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Interpreting the Influence of Race and Cognitive Activity on Neurocognition in Adults Aging with HIV

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Approximately 52%–59% of adults with HIV experience varying degrees of HIV-Associated Neurocognitive Disorder, or HAND, which can compromise their ability to perform everyday activities such as driving, managing finances, and adhering to medication regimens.^{1–5} But surprisingly, in a large cohort of women with ($n = 1,019$) and without ($n = 502$) HIV, Maki and colleagues⁶ observed that HIV alone explained a surprisingly small amount of the variance in neurocognitive performance – approximately 5% (0.05 – 0.09 SD units), less than age, race/ethnicity, annual household income, and educational level. Moreover, reading level (i.e., Wide Range Achievement Test-3, an index of educational quality) exerted the strongest effect size in explaining the differences in neurocognition, predominantly in the domains of verbal learning, verbal memory, and attention (0.15 – 0.30 SD units). Since reading level and reading ability represents a type of cognitive activity, this means that engaging in other cognitive activities may likewise be important in facilitating cognitive reserve in those with HIV, especially as they age with this disease. It is within this neurocognitive context that the study by Krueger and colleagues presented in this issue of *AIDS* is so interesting and relevant both scientifically and clinically.

When comparing older (50+) Blacks and Whites with HIV, Krueger and colleagues derived two main conclusions: 1) cognitive activity was related to neurocognitive performance, and 2) this relationship was particularly significant in Blacks. These findings are relevant to the cognitive aging and cognitive reserve literature. In their study, cognitive activity was defined as being engaged in one of nine activities (i.e., reading per day, visit museum, attend concerts, visit library, read newspaper, read magazine, time reading per year, write letter, play games). These researchers posit that engaging in stimulating cognitive activities can promote neuroplasticity that over time encourages better cognitive reserve which also facilitates better neurocognitive functioning in general. This assertion on cognitive reserve and cognitive activity is well established in animal and human research.

In animal studies, exposure to either impoverished, standard, or enriched environments is tantamount to cognitive activity. In the Enriched Environmental Paradigm studies, rats are randomized to live in one of these environments. In the impoverished environment, rats are placed in a cage in isolation with no toys or objects to explore. In the standard environment, rats are placed in a cage with two other rats, but with no toys or objects to explore. In the

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enriched environment, rats are placed with several other rats in a large cage with several toys and objects to explore; in fact, these objects are replaced with new toys and objects periodically. In several studies investigating this paradigm, researchers have found that compared to the rats in the other two conditions, rats in the enriched environment developed bigger brains, had more synaptodendritic branching, more brain derived neurotropic factors, and performed better cognitively as assessed by performance on maze tasks, all of which reflects better cognitive reserve. Similar comparisons were found between the rats in the standard environment compared to the impoverished environment, with rats in the impoverished environment experiencing the poorest outcomes. It is considered that those rats in the enriched environment experienced positive neuroplasticity, while those rats in the impoverished environment experienced negative neuroplasticity.⁷

In human studies, similar studies suggest that cognitive activity promotes better neurocognition and cognitive reserve as people age. For example, in a longitudinal study of 294 normal community-dwelling older adults, Wilson and colleagues examined the influence of early-life and late-life cognitive activity (e.g., playing a musical instrument, reading books) exerted on cognitive functioning and neuropathological burden (e.g., neocortical Lewy bodies, amyloid burden).⁸ Normal older participants received annual neurocognitive evaluations until they died, at which point an autopsy confirmed neuropathological burden. These researchers observed that accounting for some basic covariates including neuropathological burden, early- and late-life cognitive activity explained 14% of the neurocognitive impairments observed over time. Other studies in the cognitive aging literature also show that cognitive activity improves the ability to cognitive age well.^{4,9}

In a related study with 139 adults with HIV, Fazeli and colleagues examined the relationship between neurocognition and three active lifestyle factors – full-time/part-time employment, social activity, and physical activity.¹⁰ Overall, the prevalence of HAND significantly decreased as participants engaged in more of these active lifestyle factors. When one considers the cognitive activity required to engage in each of these lifestyle factors, this further confirms the value of cognitive activity on protecting one from the negative effects of HIV on neurological sequelae. In fact, there are many studies that suggest that there are many benefits of employment (i.e., social engagement, learning new skills, established routine, purpose/meaning, income) that in many ways promote positive neuroplasticity and facilitate successful cognitive aging in adults with HIV.⁵

As mentioned, Krueger and colleagues found this relationship between cognitive activity and neurocognitive function was particularly relevant for Blacks. Upon closer inspection, Whites engaged in significantly more reading per day, visiting museums, and attending concerts; activities that can be cognitively stimulating. Clearly some of these racial/ethnic differences in engagement in cognitive activities are related to socioeconomic differences in educational attainment, employment opportunities, and discretionary income to engage in such cognitive activities. Yet, some of these difference may result from educational differences observed between Blacks and Whites, especially years ago when such inequalities were more prevalent.¹¹ In a very interesting study on the role of educational quality, Crowe and colleagues examined the role of childhood educational quality on neurocognition in 433

older adults in Alabama.¹² Using the 1935 Alabama Department of Education county-level data to examine school year length, student-teacher ratio, and other indicators of educational quality, these researchers found higher student-teacher ratio (a measure of poorer educational quality) predicted poorer neurocognitive functioning while greater school year length predicted better neurocognitive functioning in both older Blacks and Whites over a 4-year period. These findings suggest that the overall cognitive activity within one's childhood educational environment may also play an important role in successful cognitive aging in those aging with HIV.¹¹

Clearly, even in lieu of HIV, other forms of cognitive activity may mitigate some of the negative neurological sequelae of HIV. For example, Krueger and colleagues found that there was a trend ($p = 0.07$) in Blacks playing more games than Whites; perhaps cognitive activities that use a gaming format would be helpful. In fact, cognitive remediation therapies have been shown to encourage positive neuroplastic changes that can promote cognitive reserve and successful cognitive aging.¹³ For example, in a sample of 46 middle-aged (40+) and older adults with HIV, Vance and colleagues randomized adults to either a speed of processing training condition or a no-contact control condition.¹⁴ Those in the speed of processing condition received up to 10 hours of cognitive activity whereby they played computer games specifically designed to improve visual attention and visual speed of processing. Compared to the control group, those adults who received this cognitive training improved on a measure of visual speed of processing; furthermore, this improved neurocognitive functioning translated to improved performance on a laboratory measure of everyday functioning. This finding is interesting given recent findings that this same type of cognitive training protocol has been shown to reduce the incidence of dementia by 33% over a 10-year period in a large cohort of normal older adults.¹⁵ Building on this science, Vance and colleagues recently began a longitudinal study to examine the dosage needed with speed of processing training to improve neurocognitive and everyday functioning in middle-aged (40+) and older adults with HIV living in the Deep South (R01MH106366-01A1 – An RCT of Speed of Processing Training in Middle-aged and Older Adults with HIV). One of the questions that can be examined from this study is whether Blacks are more amenable to and benefit from this speed of processing training compared to Whites. Given the emphasis in cognitive activity in promoting successful cognitive aging, whether it be a formalized cognitive training program or other types of cognitive activities (e.g., reading, social engagement, employment), optimism from these types of studies supports the findings from Krueger and colleagues that one can influence, to some extent, the degree to how well one can cognitively age, even with HIV.

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